

## SUPPLEMENTARY MATERIAL

### BOX 1. Stop criteria for individual patients

Participants may withdraw or be withdrawn from the study for any of the following reasons:

- A participant does not significantly meet the requirements of the protocol (e.g., a patient taking prohibited concomitant medications for an ongoing period that, in the investigator's judgment, could interfere with the interpretation of study data).
- A participant experiences an adverse reaction that, in the investigator's judgement, their participation in the study carries an unacceptable risk.
- A participant withdraws of his/her own free will (withdrawal of consent).
- A participant commits major protocol deviations.
- A patient is withdrawn at the specific request of the sponsor.

La Participants in whom the intervention has been initiated, i.e. who are at any step of the 'milk ladder', will not be replaced.

**Table 1: Recipes according to AVML levels.**

AVML LEVEL	FOOD	INGREDIENTS	RECIPE
Level 1	Cookies	<ul style="list-style-type: none"> <li>• 125 g wholemeal flour</li> <li>• 6 g powdered skimmed milk</li> <li>• 7 g dry yeast</li> <li>• 20 g sugar</li> <li>• 50 g dark chocolate chips</li> <li>• 50 g butter</li> <li>• 1 medium beaten egg</li> </ul>	<ul style="list-style-type: none"> <li>• In a bowl, mix flour, powdered milk, dry yeast, sugar and chocolate chips</li> <li>• Add in the butter and beaten egg, mixing until smooth</li> <li>• Let the dough rest in the fridge for 30 min</li> <li>• Preheat oven to 180°C (upside down)</li> <li>• Using an ice cream scoop, scoop 20 balls of dough onto a baking tray lined with parchment paper.</li> <li>• Bake for 15-20 min</li> </ul>

			<ul style="list-style-type: none"> <li>• Let them cool down on a cooking grid</li> </ul>
	Muffins	<ul style="list-style-type: none"> <li>• 250 g flour</li> <li>• 10 g dry yeast</li> <li>• 25 g sugar</li> <li>• A pinch of salt</li> <li>• 50 mL vegetal oil</li> <li>• 250 mL skimmed milk</li> <li>• 2 medium eggs</li> <li>• 1 tsp vanilla extract or 20 g low fat cocoa powder to enhance the flavour</li> </ul>	<ul style="list-style-type: none"> <li>• Preheat oven to 180°C (upside down)</li> <li>• In a bowl, whisk together the eggs and the sugar</li> <li>• Add in the oil and milk (and vanilla extract in case of using it) and mix.</li> <li>• In a different bowl, mix the flour, dry yeast and salt (and cocoa powder in case of using it). Sift it into the previous mix and combine until obtaining a homogeneous mixture</li> <li>• Spoon the batter evenly into 10 muffin pans and place them on a baking trail.</li> <li>• Bake at 180°C for 20 min or until golden brown</li> </ul>
<p>A DBPCFC with a biscuit will be performed and the parents shall be instructed to continue giving 1 biscuit per day for 15 days. After 15 days, a DBPCFC with 1 muffin will be scheduled and parents will be instructed to continue with 1 muffin per day for 3 months. Parents may alternate muffins with the commercial milk bread listed below.</p>			
<p>Commercial alternative: Milk bread buns La Bella Easo®. An OFC will be carried out with half bun of milk bread a day. After 15 days, the child will be scheduled for a new challenge with one loaf of bread milk and will continue this way for three months. Parents can alternate between commercial milk bread and muffins, without exceeding one serving of each per day.</p>			
<b>Level 2</b>	Sweet pancakes	<ul style="list-style-type: none"> <li>• 2 large eggs (73g)</li> <li>• 120 g flour</li> <li>• 25 g sugar</li> <li>• 1 tsp vanilla sugar or cinnamon (optional)</li> <li>• 20 g powdered skimmed milk</li> <li>• 45 mL water</li> <li>• 30 mL olive oil</li> <li>• A pinch of salt</li> </ul>	<ul style="list-style-type: none"> <li>• In a bowl, mix sugar and eggs</li> <li>• Add in the oil and milk and mix with an egg beater</li> <li>• Sift flour, dry yeast and salt into the previous mix and combine until obtaining a homogeneous mixture</li> <li>• Let the batter rest for 15 min</li> <li>• Heat a pan covered with oil. Spoon the batter into the pan (1 tbsp approximately) and cook on both sides over low heat</li> <li>• Repeat with all batter</li> </ul>

		<ul style="list-style-type: none"> <li>• 1 dry yeast sachet</li> </ul>	
	Salted pancakes	<ul style="list-style-type: none"> <li>• 2 large eggs (73 g)</li> <li>• 83 g flour</li> <li>• 55 g powdered skimmed milk</li> <li>• 115 mL homemade broth</li> <li>• 30 g olive oil</li> <li>• A pinch of salt</li> <li>• 1 dry yeast sachet</li> </ul>	<ul style="list-style-type: none"> <li>• In a bowl, mix milk with an egg beater</li> <li>• Sift flour, dry yeast and salt into the previous mix. Add in the oil and broth and combine until obtaining a homogeneous mixture</li> <li>• Let the batter rest for 15 min</li> <li>• Heat a pan covered with oil. Spoon the batter into the pan (1 tbsp approximately) and cook on both sides over low heat</li> <li>• Repeat with all batter</li> </ul>
	Croquettes	<ul style="list-style-type: none"> <li>• 100 g Spanish ham</li> <li>• 100 g flour</li> <li>• 100 mL olive oil</li> <li>• 1L homemade broth</li> <li>• 100 g skimmed powdered milk</li> </ul> <p>To bread and fry:</p> <ul style="list-style-type: none"> <li>• Flour</li> <li>• 3 beaten eggs</li> <li>• Olive oil</li> </ul>	<ul style="list-style-type: none"> <li>• Heat the oil in a pot over medium heat. Add in the flour, milk and ham</li> <li>• Very slowly, add in the broth stirring constantly</li> <li>• Cook the bechamel for 20 min</li> <li>• Spread the batter in a trail/recipient covered with oil or transparent film and allow to cool</li> <li>• Once cold, divide the mixture into 1-inch balls (14 units)</li> <li>• Dip the croquettes in the flour, beaten egg and coat with breadcrumbs by rolling in the bowl</li> <li>• Place the croquettes in the hot oil and fry quickly, in batches, turning several times, until golden and all the croquettes are fried</li> <li>• Remove the croquettes with a slotted spoon and set on a paper towel to absorb the excess oil</li> </ul>
Start this level with 1 sweet pancake/day. After 15 days, increase up to 2 salted pancakes or 2 croquettes/day			
<b>Level 3a<sup>†</sup></b>	Bechamel <sup>†</sup>	<ul style="list-style-type: none"> <li>• 2 cups of broth (0.5L)</li> <li>• 2 heaping tbsp of flour (50 g)</li> </ul>	<ul style="list-style-type: none"> <li>• Heat the oil in a pot over low heat. Add in the flour and the powdered skimmed milk. Mix until it is perfectly integrated</li> </ul>

		<ul style="list-style-type: none"> <li>• 4 heaping tbsp of olive/vegetable oil (40 g)</li> <li>• Powdered skimmed milk (14 g)</li> <li>• Salt</li> </ul>	<ul style="list-style-type: none"> <li>• Fry a bit and pour half of the broth (cold) slowly stirring constantly with a whisk or a wooden spoon. Mix until achieving a homogenous mixture</li> <li>• Pour the remaining broth in 2 times stirring constantly. Add salt to taste and cook the sauce over low heat for 10-15 min. The more it is cooked, the softer and tasty will be</li> </ul>
	Spanish omelette	<ul style="list-style-type: none"> <li>• 73 g egg (large egg)</li> <li>• 6,7 g powdered skimmed milk</li> <li>• 105 g potato</li> <li>• Olive/vegetable oil</li> </ul>	<ul style="list-style-type: none"> <li>• Peel and cut the potato</li> <li>• Season to taste and fry in a frying pan over medium heat for 25-30 min</li> <li>• Once fried, drain the excess of oil and keep the oil in a jar. Clean the pot with kitchen paper</li> <li>• Whisk eggs in a bowl, add in the powdered milk, solve it and then add the fried potato</li> <li>• Heat the frying pan on the stove and add a dash of the previously kept olive oil</li> <li>• Pour the egg and potato mix into the frying pan and allow the egg to cook around the edges.</li> <li>• Then, using a spatula, carefully lift up one side of the tortilla to check if the egg has slightly browned</li> <li>• Place a large dinner plate upside down over the frying pan to cover the top. With one hand on the frying pan handle and the other on top of the plate to hold it steady, quickly turn the frying pan over and the omelette will fall onto the plate</li> <li>• Carry the plate with the potato-egg mixture and empty pan back to the stove.</li> <li>• Let it cook for 3-4 minutes</li> </ul>

<b>Level 3b<sup>s</sup></b>	Bechamel <sup>n</sup>	<ul style="list-style-type: none"> <li>• 2 cups of broth (0.5L)</li> <li>• 2 heaping tbsp of flour (50 g)</li> <li>• 4 heaping tbsp of olive/vegetable oil (40 g)</li> <li>• Powdered skimmed milk (45 g; 3.5 tbsp)</li> <li>• Salt</li> </ul>	<ul style="list-style-type: none"> <li>• Heat the oil in a pot over low heat. Add in the flour and the powdered skimmed milk. Mix until it is perfectly integrated</li> <li>• Fry a bit and pour half of the broth (cold) slowly stirring constantly with a whisk or a wooden spoon. Mix until achieving a homogenous mixture</li> <li>• Pour the remaining broth in 2 times stirring constantly. Add salt to taste and cook the sauce over low heat for 10-15 min. The more it is cooked, the softer and tasty will be</li> <li>• Add 90 gr of bechamel to the vegetables</li> </ul>
	Banana Puree	<ul style="list-style-type: none"> <li>• 178 g banana (2 medium bananas)</li> <li>• 40 g corn flour (Maizena<sup>®</sup>) (3 level tbsp)</li> <li>• 50 g skimmed powdered milk (3 tbsp)</li> <li>• 0.5 L water</li> <li>• 20 g sugar (2 level tbsp)</li> <li>• 1 vanilla branch</li> </ul>	<ul style="list-style-type: none"> <li>• Put water and the vanilla branch seeds in a pan</li> <li>• Peel and cut the bananas and add them id.</li> <li>• Cook over low heat (10 min) until softened</li> <li>• Crush the mixture, add the powdered milk and corn flour and cook over low heat for 10-15 min</li> <li>• Spread around the mix (around 150 g; ½ glass) and let it cool</li> </ul>
	Fillings for the stew	<ul style="list-style-type: none"> <li>• 73 g egg (large egg)</li> <li>• 50 g breadcrumbs (3.5 tbsp)</li> <li>• 10 g skimmed powdered milk (1 level tbsp)</li> <li>• Chicken broth</li> <li>• Olive/vegetable oil</li> </ul>	<ul style="list-style-type: none"> <li>• Beat the eggs in a plate or bowl. When beaten, add the skimmed milk powder. Mix it together.</li> <li>• Add in the breadcrumbs and mix until a dough with consistency is formed.</li> <li>• Put this batter in a frying pan with plenty of hot oil over a medium heat. Leave them on one side until golden brown, turn them over and do the same on the other side. They do not take long to brown.</li> </ul>

			<ul style="list-style-type: none"> <li>• Add the stuffing to the chicken broth in a saucepan for 10-15 minutes, so that it soaks in.</li> </ul>
	French omelette	<ul style="list-style-type: none"> <li>• 73 g egg (large egg)</li> <li>• 84 mL semi-skimmed or skimmed milk or 9 g of skimmed powdered milk</li> <li>• 10 g wheat flour (1.3 level tbsp)</li> <li>• 3-4 olives** (optional)</li> <li>• Salt</li> <li>• Olive/vegetable oil</li> </ul>	<ul style="list-style-type: none"> <li>• Break the eggs and place them in a bowl, add salt and beat them with a fork</li> <li>• Add in the 52 mL of milk, flour and olives</li> <li>• Heat a tsp of oil in a frying pan, pour in the mixture when hot and shake it back and forth a few times to settle the mixture</li> <li>• Carefully and gently fold the omelette in half. Turn the omelette upside down and cook it for a few more minutes</li> </ul>
	Sweet French omelette	<ul style="list-style-type: none"> <li>• 73 g egg (large egg)</li> <li>• 84 mL semi-skimmed or skimmed milk or 9 g of skimmed powdered milk</li> <li>• 10 g corn flour (Maizena®) or wheat flour (1 level tbsp)</li> <li>• 5 g vanilla sugar (1 tsp)</li> <li>• 1 small strawberry†† (optional)</li> <li>• Olive/vegetable oil</li> </ul>	<ul style="list-style-type: none"> <li>• Break the eggs and place them in a bowl, add salt and beat them with a fork</li> <li>• Add in the 52 mL of milk, flour and strawberry pieces</li> <li>• Heat a tsp of oil in a frying pan, pour in the mixture when hot and shake it back and forth a few times to settle the mixture</li> <li>• Carefully and gently fold the omelette in half. Turn the omelette upside down and cook it for a few more minutes</li> </ul>
	Spanish omelette	<ul style="list-style-type: none"> <li>• 73 g egg (large egg)</li> <li>• 9 g skimmed powdered milk (1 level tbsp)</li> <li>• 105 g potato</li> <li>• Olive/vegetable oil</li> </ul>	<ul style="list-style-type: none"> <li>• Peel and cut the potato</li> <li>• Season to taste and fry in a frying pan over medium heat for 25-30 min</li> <li>• Once fried, drain the excess of oil and keep the oil in a jar. Clean the pot with kitchen paper</li> <li>• Whisk eggs in a bowl, add in the powdered milk, solve it and then add the fried potato</li> </ul>

			<ul style="list-style-type: none"> <li>• Heat the frying pan on the stove and add a dash of the previously kept olive oil</li> <li>• Pour the egg and potato mix into the frying pan and allow the egg to cook around the edges.</li> <li>• Then, using a spatula, carefully lift up one side of the tortilla to check if the egg has slightly browned</li> <li>• Place a large dinner plate upside down over the frying pan to cover the top. With one hand on the frying pan handle and the other on top of the plate to hold it steady, quickly turn the frying pan over and the omelette will fall onto the plate</li> <li>• Carry the plate with the potato-egg mixture and empty pan back to the stove.</li> <li>• Let it cook for 3-4 minutes</li> </ul>
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\*The selection of the milk bread brand has been made on the basis of the milk protein content. The researchers have no commercial interest in this brand. La Bella Easo® has not provided funding for this study.

†Recipes in this level provide ≈1.9 g of protein

‡ Add 90 g of bechamel to the vegetables Recipes in this level provide ≈2.6 g of protein

§ Recipes in this level provide ≈2.6 g of protein

¶Add 130 g of bechamel to the vegetables

\*\* Olives can be substituted for other ingredients to taste: sweet ham, cheese, asparagus etc.

†† Strawberries can be substituted with other fruits

**AVML**, adapted version of milk ladder; **tbsp**, tablespoon; **tsp**, teaspoon

**Table 2.** Study procedures

Procedures	Selection	Pre-intervention	Intervention (AVML)				End of the study
			LEVEL 1	LEVEL 2	LEVEL 3	LEVEL 4	
	V1	V2	V3	V4	V5	V6	V7
<b>Demographic data</b>							
Ethnicity	x						
Date of birth	x						
Sex	x						
Weight	x						
Height	x						
<b>Clinical history</b>	x	x					x
<b>Physical examination</b>	x	x	x	x	x	x	x
<b>Vital signs</b>							
SBP and DBP (mm Hg)	x	x	x	x	x	x	x
Heart rate (beats/min)	x	x	x	x	x	x	x
Oxygen saturation	x	x	x	x	x	x	x
Temperature	x	x	x	x	x	x	x
<b>Skin tests</b>	x	x					x
<b>Blood sampling</b>	x	x					x
Total IgE	x	x					x
Specific IgE	x	x					x
Specific IgG4	x	x					x
Linear IgE and IgG4 epitopes (microarray)	x	x					x
BAT		x					x
T-lymphocyte epitopes		x					x
<b>FAQLQ-PF</b>	x	x					x
<b>DBPCFC</b>		x					x
<b>OFC</b>	x		x	x	x	x	
<b>Adverse reactions</b>		x	x	x	x	x	x
<b>Concomitant medication</b>	x	x	x	x	x	x	x

AVML, adapted version of milk ladder; BAT, basophil activation test; DBP, diastolic blood pressure; DBPCFC, double-blind, placebo-controlled oral food challenge; FAQLQ-PF, Food Allergy QoL Questionnaire-Parent Form; IgE, immunoglobulin E; IgG4, immunoglobulin G4; OFC, oral food challenge; SBP, systolic blood pressure; V, visit



